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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/738,599	12/15/2000	Lisa K. Nolan	255.0001 0122	1240

26813 7590 08/10/2005

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EXAMINER

DEVI, SARVAMANGALA J N

ART UNIT PAPER NUMBER

1645

DATE MAILED: 08/10/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/738,599	Applicant(s) NOLAN ET AL.	
	Examiner S. Devi, Ph.D.	Art Unit 1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 27 May 2005.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 30-33, 37-42, 44, 45 and 67-73 ~~is/are~~ are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 30-33 and 69 ~~is/are~~ are allowed.
- 6) ☒ Claim(s) 37-42, 67, 68 and 70-73 ~~is/are~~ are rejected.
- 7) ☒ Claim(s) 44 and 45 ~~is/are~~ are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>6/27/05</u> | 6) <input checked="" type="checkbox"/> Other: <u>Sequence alignments (2)</u> |

RESPONSE TO APPLICANTS' AMENDMENT

Applicants' Amendments

- 1) Acknowledgment is made of Applicants' amendments filed 05/27/05 and 04/27/05 in response to the non-final Office Action mailed 01/27/05.

Status of Claims

- 2) Claims 30-33, 37, 44, 45 and 67-70 have been amended via the amendment filed 04/27/05.

New claims 71-73 have been added via the amendment filed 04/27/05.

Claims 30-33, 35-42 and 44-73 are pending.

Claims 30-33, 37-42, 44, 45 and 67-73 are under examination.

Prior Citation of Title 35 Sections

- 3) The text of those sections of Title 35 U.S. Code not included in this action can be found in a prior Office Action.

Prior Citation of References

- 4) The references cited or used as prior art in support of one or more rejections in the instant Office Action and not included on an attached form PTO-892 or form PTO-1449 have been previously cited and made of record.

Information Disclosure Statement

- 5) Acknowledgment is made of an Information Disclosure Statement filed on 05/27/05. The information referred to therein has been considered and a signed copy of the same are attached to this Office Action.

Objection(s) Withdrawn

- 6) The objection to claims 30-33, 44, 45, 69 and 70 made in paragraph 21 of the Office Action mailed 01/27/05 is withdrawn in light of Applicants' amendment to the claims.

Rejection(s) Maintained

- 7) The rejection of claim 70 made in paragraph 11 of the Office Action mailed 07/30/04 and maintained in paragraph 17 of the Office Action mailed 01/27/05 under 35 U.S.C § 112, first

paragraph, as containing new subject matter, is maintained for reasons set forth therein.

Applicants submit that the immunogenic fragments or subunits are of the peptides rather than the nucleic acid. Applicants state that support for immunogenic fragments or immunogenic subunits of an *E. coli* Iss polypeptide is found at pages 47-49 of the specification.

Applicants' arguments have been considered, but are not persuasive. Unlike the limitations in claims 37 and 68: 'immunogenic fragment or immunogenic subunit of the avian *E. coli* Iss polypeptide', the generic and confusing limitation in claim 70: 'an immunogenic fragment or immunogenic subunit thereof' still encompasses an immunogenic fragment or immunogenic subunit of the isolated nucleic acid molecule. It is noted that amendments similar to the one made to claims 37 and 68 have not been made to claim 70. The specification, as originally filed, does not provide descriptive support for an 'immunogenic subunit' or 'immunogenic fragment' of the isolated nucleic acid molecule. The rejection stands.

8) The rejection of claim 70 made in paragraph 12(a) of the Office Action mailed 07/30/04 and maintained in paragraph 18 of the Office Action mailed 01/27/05 under 35 U.S.C § 112, second paragraph, as being indefinite, is maintained for reasons set forth therein.

Applicants submit that as fragments and subunits are not indefinite with regard to the polypeptide, the rejection should be withdrawn.

However, as presented currently, the claim does not recite that the 'immunogenic fragment' or 'immunogenic subunit thereof' is of the polypeptide, or of the avian *E. coli* Iss polypeptide. Instead, the claim includes an immunogenic fragment or immunogenic subunit of the isolated nucleic acid molecule. The rejection stands.

Rejection(s) Withdrawn

9) The rejection of claims 37-42, 44, 45 and 67-70 made in paragraph 19 of the Office Action mailed 01/27/05 under 35 U.S.C § 112, first paragraph, as being non-enabled with regard to the scope, is withdrawn upon further consideration.

10) The rejection of claim 37 made in paragraph 20(a) of the Office Action mailed 01/27/05 under 35 U.S.C § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the claim.

11) The rejection of claim 68 made in paragraph 20(a) of the Office Action mailed 01/27/05

under 35 U.S.C § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the claim.

12) The rejection of claim 41 made in paragraph 20(b) of the Office Action mailed 01/27/05 under 35 U.S.C § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the base claim.

13) The rejection of claim 67 made in paragraph 20(c) of the Office Action mailed 01/27/05 under 35 U.S.C § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the base claim.

14) The rejection of claim 67 made in paragraph 20(d) of the Office Action mailed 01/27/05 under 35 U.S.C § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the claim.

15) The rejection of claims 38-42, 44, 45 and 67 made in paragraph 20(e) of the Office Action mailed 01/27/05 under 35 U.S.C § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the base claim.

Rejection(s) under 35 U.S.C § 112, First Paragraph (New Matter)

16) Claims 71-73 are rejected under 35 U.S.C § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Claims 71-73 are directed to the immunogenic composition as claimed in claim 69 or 70 comprising the specifically recited nucleotide sequences 'wherein the promoter is a eukaryotic promoter and the polypeptide is expressed in an animal cell'; and 'wherein the promoter is a eukaryotic promoter and the nucleic acid molecule forms an expression vector suitable for use in an animal cell'. Applicants point to pages 28-29, lines 1-4 of the specification as providing descriptive support for the new claims. However, there is no descriptive support in this part of the specification for such as product comprising the specifically recited nucleotide sequences and a eukaryotic promoter wherein the recited polypeptide, or immunogenic fragment or immunogenic subunit thereof is expressed in an animal cell, or wherein the eukaryotic promoter and the nucleic acid

molecule forms an expression vector suitable for use in an animal cell, as recited. Therefore, the limitations in the claims are considered to be new matter. *In re Rasmussen*, 650 F2d 1212 (CCPA, 1981). New matter includes not only the addition of wholly unsupported subject matter but also, adding specific percentages or compounds after a broader original disclosure, or even omission of a step from a method. See M.P.E.P 608.04 to 608.04(c).

Applicants are respectfully requested to remove the new matter from the claims, or to point to specific pages and line numbers in the originally filed specification where support for the above-identified limitations can be found.

Rejection(s) under 35 U.S.C § 112, Second Paragraph

17) Claims 71 and 73 are rejected under 35 U.S.C § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention.

(a) Claims 71 and 73 are vague and confusing in the limitation: ‘an immunogenic fragment or immunogenic subunit thereof’, because it is unclear whether the recited ‘immunogenic fragment or immunogenic subunit thereof’ is a subunit or fragment of ‘the polypeptide’, or of the ‘avian *E. coli* Iss polypeptide’.

(b) Claim 73 is vague, indefinite and/or lacks antecedent basis in the limitation: ‘an avian *E. coli* Iss polypeptide or an immunogenic fragment or immunogenic subunit thereof’. Claim 73 depends from claim 70, which already recites ‘an avian *E. coli* Iss polypeptide or an immunogenic fragment or immunogenic subunit thereof’. Is the one recited in claim 73 different from the one recited in the base claim?

Applicants’ Arguments Noted

18) In response to a previous art rejection, Applicants submitted the following arguments:

Independent claims 37 and 68 each recite an ‘immunogenic composition’ which is defined at lines 19-24 of page 43 of the specification as referring ‘to a composition or preparation administered in an amount effective to raise antibodies in a recipient and further provides some therapeutic benefit or effects so as to result in an immune response that inhibits or prevents a septicemic disease in a subject, or so as to result in the production of antibodies to a virulent complement resistant avian *E. coli* isolate, or polypeptide or peptide employed as an

immunogen'. At page 10 of Applicants' response filed 11/01/04, Applicants further alleged the following:

The Examiner has not provided any evidence as to why the nucleotide sequence cited in the Action inherently serves as an immunogenic composition. Specifically, the Examiner provides no evidence that the nucleotide sequence cited in the Action encodes a polypeptide that provides some therapeutic benefit or effect so as to result in an immune response that inhibits or prevents a septicemic disease in a subject, in order to support reliance on a theory of inherency under 35 U.S.C. 102(b).

However, in the response filed 04/27/05, Applicants now argue that the claimed immunogenic composition is not required to provide a therapeutic benefit or effect, and that immunogenicity within the specification is defined both in the therapeutic and non-therapeutic context of stimulating antibody formation. See paragraph bridging pages 11 and 12 of Applicants' response filed 04/27/05. Based on this current position, art rejections have been set forth below.

Rejection(s) under 35 U.S.C § 103

19) Claims 37-40, 67 and 68 are rejected under 35 U.S.C § 103(a) as being unpatentable over Barondess *et al.* (*Nature* 344: 871-874, 1990, already of record) (Barondess, 1990) in view of Harlow *et al.* (*In: Antibodies: A laboratory Manual*. Cold Spring Harbor Laboratory, Chapter 5, p. 76, 1988, already of record).

It is noted that lines 1 and 2 of page 49 of the specification define an 'immunogenic subunit of an *E. coli* Iss polypeptide' as 'a subunit that elicits an immune response in a subject to which it is administered'. At paragraph bridging pages 7 and 8, 'an immunogenic composition' comprising a nucleic acid molecule encoding an *E. coli* Iss polypeptide is described as one which on 'administration to a subject induces the production of antibodies to said polypeptide'. The specification herein states that the produced antibodies 'can' (but not required to) inhibit or block subsequent infection of the host by a complement resistant and/or virulent avian *E. coli*.

Barondess *et al.* (1990) disclosed an isolated nucleic acid molecule comprising several long stretches of nucleotides showing 100% sequence identity with nucleotides 73 to 309 of SEQ ID NO: 22, plasmids, vectors, phages, and host cells comprising the same. See the sequence search reports; and Figure 1 of Barondess *et al.* (1990). Barondess *et al.* (1990) taught an isolated *bor* gene sequence which encodes an envelope protein, gene fusions, fragments thereof, and fusions expressed in lysogens (see pages 871 and 872; and Fig 1 and Figure 1 legend). The fusion fragments were subcloned and sequenced. The fragments of Barondess'

nucleic acid molecule are expected to encode a fragment of a polypeptide that is long enough to serve as an immunogenic fragment or immunogenic subunit on administration to a subject. For instance, the polypeptide fragment or subunit encoded by Barondess' nucleotide sequence encoding the polypeptide fragment or subunit,

KTVDAAKICGGAENVVKTETQQTFFVNGLLGFIT, is long enough to be immunogenic, given the art-known fact that a polypeptide fragment of a full length protein that is at least 6 amino acid-long is sufficiently long to be immunogenic to induce an antibody response in a subject (see page 76 of Harlow *et al.*). The fact that Barondess' polypeptide fragment or subunit was expressed or encoded indicates that Barondess' nucleic acid molecule further comprised a regulatory sequence, a control sequence, or a promoter operably linked to the nucleotide sequence.

Barondess *et al.* (1990) do not expressly teach their isolated nucleic acid molecule being present in a pharmaceutically acceptable carrier.

However, it was conventional and routine in the art to add a pharmaceutical composition to an art-known nucleic acid to produce a composition as claimed.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to add an art-known pharmaceutical carrier to Barondess' (1990) nucleic acid to produce the instant invention with a reasonable expectation of success. One of ordinary skill in the art would have been motivated to produce the instant invention for the expected benefit of providing Barondess' (1990) nucleic acid as an immunogenic composition, since it is conventional in the art to add an art-known carrier to an art-known nucleic acid to facilitate its use for diagnostic or pharmaceutical purposes. Addition of an art-known pharmaceutically acceptable carrier to an art-known isolated nucleic acid is well within the realm of routine experimentation.

Claims 37-40, 67 and 68 are *prima facie* obvious over the prior art of record.

20) Claim 41 is rejected under 35 U.S.C § 103(a) as being unpatentable over Barondess *et al.* (Nature 344: 871-874, 1990, already of record) (Barondess *et al.*, 1990) as applied to claim 37 above and further in view of Applicants' admitted state of the prior art.

The teachings of Barondess *et al.* (1990) are explained above which do not expressly

disclose that the polypeptide was expressed in an animal cell.

However, the expression of an art-known nucleic acid molecule via an art-known regulatory or control sequence that causes expression in an art-known animal cell line was routine and conventional in the art at the time of the invention. For instance, Applicants acknowledge in the instant specification the following to be known in the art: transformation and transfection methods; a wide variety of control or promoter sequences, compatible vectors, and eukaryotic expression systems or cell lines known to those skilled in the art of molecular biology to express polynucleotides; the use of vaccinia recombinant plasmid; the production of fusion protein for easy purification; and the standard affinity chromatography and purification methods. See pages 28-34 of the specification.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to express Barondess' (1990) isolated nucleic acid molecule or polynucleotide via any one of the admittedly art-known animal or mammalian cell using any one of the admittedly art-known compatible control or regulatory sequences or eukaryotic promoters using art known techniques to produce the instant invention, with a reasonable expectation of success. Expression of Barondess' (1990) nucleic acid via an animal cell is well within the realm of routine experimentation. One of skill in the art would have been motivated to produce the instant invention for the expected benefit of improved expression of Barondess' polynucleotide since improved expression is ideally desired in the art.

Claim 41 is *prima facie* obvious over the prior art of record.

21) Claim 42 is rejected under 35 U.S.C § 103(a) as being unpatentable over Barondess *et al.* (*Nature* 344: 871-874, 1990, already of record) (Barondess *et al.*, 1990) as applied to claim 38 above and further in view of Krieg *et al.* (WO 96/02555, already of record).

The teachings of Barondess *et al.* (1990) are explained above, which do not disclose the their polynucleotide further comprising an immunostimulatory sequence.

However, the use of immunostimulatory sequences, for example, an immunostimulatory oligonucleotide sequence along with a heterologous polynucleotide sequence for the purpose of immunostimulation was well known in the art at the time of the invention. For instance, Krieg *et al.* showed that it was routine and conventional in the art to use a CpG immunostimulatory

nucleotide sequence in a pharmaceutical composition (see abstract; and claims).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to express Barondess' (1990) nucleic acid molecule together with Krieg's immunostimulatory oligonucleotide sequence to produce the instant invention with a reasonable expectation of success. Given Krieg's teaching of the routine and conventional nature of using an immunostimulatory oligonucleotide in a pharmaceutical composition for the purpose of immunostimulation, one of ordinary skill in the art would have been motivated to produce the instant invention for the expected benefit of further enhancing the immune response to Barondess' (1990) product.

Claim 42 is *prima facie* obvious over the prior art of record.

Remarks

22) Claims 37-42, 67, 68 and 70-73 stand rejected. Claims 30-33 and 69 contain allowable subject matter. Claims 44 and 45 are objected to for being dependent from a rejected claim.

23) Papers related to this application may be submitted to Group 1600, AU 1645 by facsimile transmission. Papers should be transmitted via the PTO Fax Center, which receives transmissions 24 hours a day and 7 days a week. The transmission of such papers by facsimile must conform with the notice published in the Official Gazette, 1096 OG 30, November 15, 1989. The Fax number for submission of amendments, responses or papers is (571) 273-8300.

24) Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAG or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.Mov>. Should you have questions on access to the Private PAA system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).


25) Any inquiry concerning this communication or earlier communications from the Examiner should be directed to S. Devi, Ph.D., whose telephone number is (571) 272-0854. A message may be left on the Examiner's voice mail system. The Examiner can normally be reached on Monday to Friday from 7.15 a.m. to 4.15 p.m. except one day each bi-week, which would be disclosed on the Examiner's voice mail system.

Application SN: 09/738,599
Art Unit: 1645

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Lynette Smith, can be reached on (571) 272-0864.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

August, 2005


S. DEVI, PH.D.
PRIMARY EXAMINER

ALIGNMENTS

RESULT 1

BOR_LAMBDA

ID BOR_LAMBDA STANDARD; PRT; 97 AA.

AC P26814;

DT 01-AUG-1992 (Rel. 23, Created)

DT 01-AUG-1992 (Rel. 23, Last sequence update)

DT 10-OCT-2003 (Rel. 42, Last annotation update)

DE Bor lipoprotein precursor.

GN BOR.

OS Bacteriophage lambda.

OC Viruses; dsDNA viruses, no RNA stage; Caudovirales; Siphoviridae;

OC Lambda-like viruses.

OX NCBI_TaxID=10710;

RN [1]

RP SEQUENCE FROM N.A.

RX MEDLINE=83189071; PubMed=6221115;

RA Sanger F., Coulson A.R., Hong G.F., Hill D.F., Petersen G.B.;

RT "Nucleotide sequence of bacteriophage lambda DNA.";

RL J. Mol. Biol. 162:729-773(1982).

RN [2]

RP CHARACTERIZATION.

RX MEDLINE=90363299; PubMed=2144037;

RA Barondes J.J., Beckwith J.;

RT "A bacterial virulence determinant encoded by lysogenic coliphage

RT lambda.";

RL Nature 346:871-874(1990).

CC -1- FUNCTION: Not known; is expressed during lysogeny in Escherichia

CC coli.

CC -1- SUBCELLULAR LOCATION: Attached to the membrane by a lipid anchor

CC (Probable).

CC -1- SIMILARITY: TO PLASMID INCFI COLV2-K94 ISS PROTEIN.

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DR EMBL; X55792; CAA39317.1; -

DR InterPro: IPR000437. Description

DR PROSITE; PS00013; PROKAR LIPOPROTEIN; 1.

KW Lipoprotein; Membrane; Signal; Palmitate.

FT SIGNAL 1 16 POTENTIAL.

FT CHAIN 17 97 BOR LIPOPROTEIN.

FT LIPID 17 17 8-diacylglycerol cysteine (in host)

FT LIPID 17 17 (Potential).

FT LIPID 17 17 N-palmitoyl cysteine (in host)

FT LIPID 17 17 (Potential).

SQ SEQUENCE 97 AA; 10386 MW; 45CDAE2A5A48FF1E CRC64;

Alignment Scores:

Pred. No.: 8.97e-39

Score: 381.00

Percent Similarity: 94.87%

Best Local Similarity: 93.59%

Query Match: 84.11%

DB: 1

Length: 97

Matches: 73

Conservative: 1

Mismatches: 4

Indels: 0

Gaps: 0

US-09-738-599-22_COPY_73_309 (1-237) x BOR_LAMBDA (1-97)

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QY      61 CATTTCTTCGTTTCGGGAATTGGACAAGAGAAAACCTGTTGATGCAGCCAAAATTGTGGC 120
DB      40 HisPhePheValSerGlyIleGlyGlnLysLysThrValAspAlaAlaLysIleCysGly 59

QY     121 GGTGCAGAAAATGTTGTTTAAACAGAAAACCTAGCAAACATTCGTAATGGATTGCTCGGT 180
DB      60 GlyAlaGluAsnValValLysThrGluThrGlnGlnThrPheValAsnGlyLeuLeuGly 79

QY     181 TTTATCACTTTTGGCATCTATACTCCGCTGGAAGCCCGGTATATTGCTCACA 234
DB      80 PheIleThrLeuGlyIleTyrThrProLeuGluAlaArgValTyrCysSerGln 97

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73-309 07
SEQ ID NO.22

